General

Guideline Title

WHO guidelines: use of cryotherapy for cervical intraepithelial neoplasia.

Bibliographic Source(s)

World Health Organization (WHO). WHO guidelines: use of cryotherapy for cervical intraepithelial neoplasia. Geneva (Switzerland): World Health Organization (WHO); 2011. 28 p. [94 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The definitions for the quality of the evidence (++++, +++0, ++00, +000) and the strength of the recommendations (strong, conditional) are provided at the end of the "Major Recommendations" field.

Use of Cryotherapy for Prevention of Cervical Intraepithelial Neoplasia (CIN)

1a. The expert panel recommends cryotherapy over no treatment (strong recommendation, +000 quality evidence).

Remarks: This recommendation is strong, despite the presence of very-low-quality evidence. The expected benefit of cervical cancer prevention is very high but there is uncertainty related to the occurrence of adverse outcomes. There was very low-quality evidence for the occurrence of spontaneous abortions and infertility but the risk appeared similar to that in the general population. Although neither the risk of human immunodeficiency virus (HIV) acquisition in HIV-negative women nor the risk of HIV transmission by HIV-infected women who undergo cryotherapy is known, the current limited data do not suggest that there is an increase in the risk of HIV acquisition/transmission. Additional data regarding the rate of HIV acquisition/transmission are pending and will need to be assessed in future. However, the panel agreed that the net benefit from cryotherapy outweighs the potential HIV risk.

1b. In settings where loop electrosurgical excision procedure (LEEP) is available and accessible, the expert panel suggests treatment with LEEP over cryotherapy (conditional recommendation, ++00 quality evidence).

Remarks: This recommendation applies to women regardless of HIV status. The benefits of LEEP when compared to cryotherapy were greater, and harms fewer or similar; therefore, LEEP was suggested. However, the panel recognized that there are greater resource implications for LEEP than with cryotherapy and therefore LEEP is not available in all settings. When LEEP is unavailable, cryotherapy is recommended (see recommendation 1a). Although the risk of HIV seroconversion in HIV-negative women, and the risk of transmission after LEEP or cryotherapy

are unknown, the benefits of LEEP were felt to outweigh the harms, and, therefore, this recommendation applies to women regardless of HIV status.

Lesion Size

2. Among women with CIN lesions covering more than 75% of the ectocervix, or with lesions extending beyond the cryo tip being used, the expert panel suggests performing or referring for excisional therapy (conditional recommendation, ++00 quality evidence).

Remarks: This recommendation includes considerations that cryo tips should cover the entire lesion and that the largest cryo tip typically only covers lesions that extend over up to 75% of the cervix. Since the quality of the evidence is low for recurrent CIN lesions and for lesions larger than 75% of the cervical surface, the panel made a conditional recommendation.

Lesions Extending into the Endocervical Canal

In women with CIN lesions extending into the endocervical canal, prior guidelines recommend excisional procedures; this panel operated under this assumption.

3a. In settings where LEEP is available and accessible, and women present with CIN lesions extending into the cervical canal, the expert panel suggests treatment with LEEP over cryotherapy (conditional recommendation, ++00 quality evidence).

Remarks: The benefits of LEEP were greater than those of cryotherapy, and the harms were fewer in these women. However, since there are greater resource implications for LEEP than cryotherapy, and thus LEEP is not available in all settings, a conditional recommendation was made.

3b. In settings where excisional procedures (e.g. LEEP, laser or cold knife conization [CKC]) or referral to additional treatment are not available, the expert panel suggests that women with lesions extending into the endocervical canal be treated with cryotherapy (conditional recommendation, +000 quality evidence).

Remarks: The risk of treatment failure is higher in women with CIN lesions extending into the cervical canal than in women whose lesion margins are clearly demarcated or do not extend into the cervical canal. The rationale for treating these women is that women left untreated may be lost to follow-up (i.e., they may not receive further treatment and are at risk for developing cervical cancer). This recommendation should be considered in the context of recommendation 3a.

Cryotherapy Technique and Procedure

4. The expert panel suggests double freeze using a 3 minute freeze, 5 minute thaw, 3 minute freeze cycle over single-freeze cryotherapy (conditional recommendation, ++00 quality evidence).

Remarks: The evidence stems from studies in which a single-freeze technique was performed for up to 3 minutes. This recommendation takes into consideration that during a cryotherapy procedure, the iceball should extend beyond the edge of the cryo tip. Data from trials regarding the benefits and harms of single-freeze versus double-freeze techniques are pending and will be assessed in the future. The panel commented that randomized controlled trials should be performed to specifically address this issue.

5. The expert panel recommends cryotherapy using either carbon dioxide (CO_2) or nitrous oxide (N_2O) gas (strong recommendation, ++00 quality evidence); in settings where both gases are available, the expert panel suggests cryotherapy with CO_2 rather than with N_2O (conditional recommendation, +000 quality evidence).

Remarks: Due to the limitations in the available evidence, it is uncertain whether CO_2 provides better or worse health outcomes, but the existing evidence suggests that there is no difference. Laboratory studies suggest no difference in temperature at the cryo tip between different grades of CO_2 (e.g., medical or industrial). Although, N_2O gas is less available and requires more resources due to higher cost and additional requirements for ventilation, in settings where N_2O gas is more likely to be available or has other advantages, this conditional recommendation suggests that N_2O gas may be used. Studies addressing the use of CO_2 versus N_2O are being conducted.

6. The expert panel recommends that the "cough technique" should not be used during cryotherapy (strong recommendation, +000 quality evidence).

Remarks: The "cough" or "freeze–clear–freeze" technique was historically used because of technical deficiencies in a particular cryotherapy device from a single manufacturer, which caused instrument clogging. This device has been removed from the market, and so this is a strong recommendation despite very low-quality evidence.

7. The expert panel suggests that prophylactic antibiotics should not be used when providing cryotherapy (conditional recommendation, +000 quality evidence).

Remarks: While there may be fewer minor adverse events and fewer minor infections with prophylactic antibiotic use, there is a risk of increased antimicrobial resistance and allergic reactions that is unlikely to outweigh any potential benefits. Resources also appear to be increased with the use of antibiotics.

Providers

8. The expert panel recommends that healthcare workers (including non-physicians) trained in cryotherapy perform the procedure for women when it is indicated (strong recommendation, ++00 quality evidence); the expert panel also suggests that trained nurses or trained midwives rather than physicians may perform cryotherapy (conditional recommendation, +000 quality evidence).

Remarks: The importance of cryotherapy training of the health-care worker was considered when making this recommendation. There appear to be better health outcomes when cryotherapy is performed by trained nurses or trained midwives rather than physicians. However, values and preferences for cryotherapy performed by physicians versus midwives or nurses differ across settings. In many settings, the resources required for nurses and midwives are lower than for physicians.

Use of Cryotherapy During Pregnancy

9a. In pregnant women, the expert panel suggests deferring cryotherapy until after pregnancy (conditional recommendation, +000 quality evidence).

Remarks: Deferral means that cryotherapy is delayed until the postpartum period. The available limited evidence does not suggest that cryotherapy increases risk of adverse pregnancy outcomes when performed during pregnancy; however, an increased risk of pregnancy loss cannot be ruled out and evidence is required. If women with histologically confirmed CIN lesions are at a high risk of loss to follow-up, or if additional opportunities for treatment are unlikely, treatment during pregnancy may be considered. However, there is an opportunity for enforcing the need for postpartum visits (including opportunities for child vaccination) if lesions are identified during pregnancy. There also are possible negative perceptions if cryotherapy is (erroneously) associated with pregnancy loss by women.

9b. In women whose pregnancy status is unknown (or there is no clinical evidence of pregnancy), the expert panel suggests using cryotherapy (conditional recommendation, +000 quality evidence).

Remarks: This is based on recommendation 1a.

Retreatment of CIN Lesions with Cryotherapy

10a. The expert panel recommends cryotherapy over no treatment for women who screen positive after prior cryotherapy treatment (strong recommendation, +000 quality evidence).

Remarks: There was no evidence for use of cryotherapy over no treatment in women who screen positive after previous treatment with cryotherapy. Therefore, this recommendation is based on recommendation 1a.

10b. In settings where LEEP is available and accessible, the expert panel suggests treatment with LEEP over cryotherapy for women who screen positive after prior cryotherapy treatment (conditional recommendation, ++00 quality evidence).

Remarks: There was very-low-quality evidence for benefits of LEEP techniques over cryotherapy and no evidence for harm in women who screen positive after previous treatment with cryotherapy. This recommendation is directly related to recommendation 1b.

Education

As part of best practice, detailed counselling and education should be provided with informed consent, prior to performing cryotherapy. Specific involvement of a woman's partner post-treatment should be given special attention, and, in particular, the use of condoms post-cryotherapy. The reviewed evidence was judged by the expert panel as too indirect to make a recommendation for additional education and counselling beyond what would be part of best practice. Evidence from future interventions may inform this question.

Definitions:

Assessment of the Strength of the Recommendation

In keeping with WHO guideline terminology, the recommendations are either "strong" or "conditional". For strong recommendations, the guideline

uses the words "the Expert Panel recommends", and for conditional recommendations, "the Expert Panel suggests". Suggested interpretations of "strong" and "conditional" recommendations are provided in the table below. Understanding the interpretation of these two grades – either strong or conditional – is essential for health-care decision-making.

Interpretation of Strong and Conditional Recommendations

Implications	Strong Recommendation	Conditional Recommendation
For patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
	Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that the clinician must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful for helping individuals make decisions consistent with their values and preferences.
For policymakers	The recommendation can be adopted as policy in most situations.	Policy-making will require substantial debate and involvement of various stakeholders.

Quality of Evidence

Grade	Definition
++++	High quality: Further research is very unlikely to change confidence in the estimate of effect.
+++0	Moderate quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
++00	Low quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
+000	Very low quality: Any estimate of effect is very uncertain.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Cervical epithelial neoplasia (CIN)

Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Nursing

Obstetrics and Gynecology

Oncology

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To summarize the new evidence-based World Health Organization (WHO) recommendations about the use of cryotherapy in women with histologically confirmed cervical intraepithelial neoplasia (CIN) for low-, middle- and high-income countries

Target Population

Women with suspected or confirmed cervical epithelial neoplasia

Interventions and Practices Considered

1. Cryotherapy
2. Loop electrosurgical excision procedure (LEEP)
3. Performing or referring for excisional therapy
4. Cryotherapy technique and procedure
    - Single freeze versus double freeze
    - Carbon dioxide versus nitrous oxide
    - Use of "cough" technique (not recommended)
    - Use of prophylactic antibiotics (not recommended)
5. Use of trained nonphysician healthcare workers (nurses, midwives) to perform cryotherapy
6. Retreatment of cervical intraepithelial neoplasia (CIN) with cryotherapy
7. Patient counseling and education

Major Outcomes Considered

- Recurrence rates of cervical intraepithelial neoplasia (CIN)

- Major and minor adverse events
- Cervical cancer incidence
- Mortality

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

MEDLINE, EMBASE, LILACS, The Cochrane Library and the WHO Clinical Trials Search Portal were searched up to July 2009, using key subject and text words for cryotherapy and cervical cancer, depending on the database (see Appendix A in the original guideline document for the MEDLINE search strategy). The search was not limited by language or by study type. The evidence review team screened titles, abstracts and full text of potentially relevant literature, in duplicate. The first screen was for controlled trials (randomized or non-randomized), but because only a few controlled trials were identified, observational studies without independent controls were also included as evidence. Authors in the field, and the expert guideline panel, were also contacted to identify missing studies, studies in progress or studies not yet published.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

Grade	Definition
++++	High quality: Further research is very unlikely to change confidence in the estimate of effect.
+++0	Moderate quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
++00	Low quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
+000	Very low quality: Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

An independent group of scientists at a World Health Organization (WHO) collaborating centre conducted systematic reviews and produced evidence summaries following the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach. GRADE evidence profiles were created for 16 key questions about the effects of cryotherapy in the presence of histologically confirmed cervical intraepithelial neoplasia (CIN) compared to no treatment and to loop electrosurgical excision procedure (LEEP), as well as the use of different techniques of cryotherapy.

Preparation of the Evidence Profiles and Grading of the Evidence

The evidence review team conducted a series of systematic literature reviews following the methods of the Cochrane Collaboration, and prepared GRADE evidence profiles for each question. During this process, the steering group held conference calls to discuss issues about the available evidence, the presentation of the results, and their impact on making recommendations.

When possible, relative effects (such as relative risks and odds ratios of an event) were calculated from pooled data of controlled studies. When there were no data, indirect comparisons were made (e.g. randomized controlled studies of cryotherapy versus laser excision were compared to laser excision versus LEEP), and a network meta-analysis was conducted. In studies without independent controls, the risks of an event were pooled across studies (e.g., for cryotherapy and for LEEP), and a relative effect was then calculated to compare those pooled results. All results were normalized to effects over a period of one year, with the exception of adverse events, most of which would probably occur and be reported within one year. Cervical cancer rates in untreated CIN were obtained from one reference and annualized. It was assumed that these risks were constant over time.

Evidence summaries and profiles, which were based on the evidence of the systematic reviews, were prepared for each question using the GRADEprofiler software. GRADE evidence profiles present the effect of the intervention on each outcome (e.g., number of women with recurrent CIN), and the quality of the evidence for each outcome. The quality of a body of evidence is assessed based on the following criteria: risk of bias, imprecision, inconsistency, indirectness, publication bias, magnitude of effect, dose–effect relations and an assessment of the effect of residual confounding and bias. Quality is categorized into four levels, ranging from +000, being the lowest quality, to ++++, being the highest quality (see the "Rating Scheme for the Strength of the Evidence" field). The GRADE evidence profiles allow the expert guideline panel to base its judgments on the same concisely summarized evidence when making recommendations.

GRADE evidence profiles were created for 16 key questions about the effects of cryotherapy compared with no treatment or LEEP in women with histologically confirmed CIN1, 2 or 3 (see Appendix B in the original guideline document for summary tables for each recommendation; GRADE tables are available from http://www.who.int/reproductivehealth/publications/cancers/9789241502856/en/index.html). The systematic reviews found only a few randomized controlled trials or controlled observational studies (such as cohort or case–control studies) that fulfilled the inclusion criteria. Therefore, most of the recommendations are based on pooled results across observational studies of women who received cryotherapy. For these analyses, results were pooled across all CIN grades (CIN1, 2, 3), and, when possible, tested for differences between outcomes for CIN1 and CIN2/3.

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Description of Methods Used to Formulate the Recommendations

The methods used to develop these guidelines follow the World Health Organization (WHO) handbook for guidelines development (see the "Availability of Companion Documents" field).

Formulating Questions and Determining Outcomes

In March 2009, experts invited by WHO drafted a list of 45 general questions about the effects of cryotherapy in women with cervical intraepithelial neoplasia (CIN). These experts were then asked to rank the questions by priority.

Expert Guideline Panel

WHO selected a multidisciplinary expert guideline panel comprising clinicians with cryotherapy experience, researchers in cervical cancer prevention and treatment, programme directors, epidemiologists, public health officers and methodologists. The methodologists (evidence review team) were based at the McMaster University WHO Collaborating Center and had expertise in guideline development and evidence synthesis. A steering group of seven members was then created from the expert guideline panel, to guide the process.

Following a review of the suitability of an initial 45 general questions, these questions were refined to 16 questions for which an evidence review was deemed necessary. The steering group also decided to assess the evidence for the effects of cryotherapy in women with histologically confirmed CIN, to provide the best estimate of the benefits and side-effects of cryotherapy without the potential for confounding the outcomes due to false-positive screening tests or diagnoses.

To determine the outcomes, a scoping review of cryotherapy studies was conducted by the evidence review team. The expert guideline panel was also consulted. A list of outcomes to be considered when making the recommendations was compiled. Nineteen members of the expert guideline panel independently and anonymously scored the outcomes by importance for decision-making, via an electronic survey. The mean and median importance of each outcome (scale: 1 – least important to 9 – critical) was calculated, and 16 outcomes were identified as important or critical (see Box 1 in the original guideline document).

One week before the expert guideline panel met to develop the recommendations, panel members were able to review the evidence profiles for each question via a password-protected electronic SharePoint site.

Development of Recommendations

The expert guideline panel met on 22 to 23 September 2010, to review the evidence and make recommendations. This meeting was chaired by a methodologist with experience in guideline development, and cochaired by a gynaecological oncologist. There were 32 panel experts, as well as WHO and International Agency for Research on Cancer (IARC) officers, who provided scientific input and guidance. The key objectives of the meeting were to formulate evidence-based recommendations for each of the priority questions, identify key research gaps and discuss a dissemination plan for the new guidelines.

During the September meeting, the panel developed recommendations based on the GRADE evidence profiles. For each recommendation, the panel considered and agreed on the following: the quality of the evidence; the balance of benefits and downsides; the assumptions about the values and preferences associated with the decision; and the extent of resource use. Recommendations were made by consensus. Before the meeting concluded, the panel used the evidence to classify each recommendation as "strong" or "conditional" and agreed on the wording and remarks for each recommendation.

Cryotherapy outcomes stratified by CIN grade at diagnosis were not different enough to make separate recommendations based on CIN grade. For this reason, these recommendations can apply to any CIN grade. There were few studies measuring outcomes that the panel identified as critical to decision-making: fertility and obstetrics outcomes; maternal morbidity; acceptability of the procedure to women or their health-care providers; referrals rates for complications; and HIV acquisition and transmission. Therefore, the recommendations are based primarily on studies that measured cryotherapy treatment failures for CIN (i.e., included any evidence of disease after treatment); major and minor adverse events; and mortality.

Rating Scheme for the Strength of the Recommendations

Assessment of the Strength of the Recommendation

In keeping with WHO guideline terminology, the recommendations are either "strong" or "conditional". For strong recommendations, the guideline uses the words "the Expert Panel recommends", and for conditional recommendations, "the Expert Panel suggests". Suggested interpretations of "strong" and "conditional" recommendations are provided in the table below. Understanding the interpretation of these two grades – either strong or conditional – is essential for health-care decision-making.

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Implications	Strong Recommendation	Conditional Recommendation
	and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that the clinician must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful for helping individuals make decisions consistent with their values and preferences.
For policymakers	The recommendation can be adopted as policy in most situations.	Policy-making will require substantial debate and involvement of various stakeholders.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for most recommendations (see the "Major Recommendations" field).

Most of the recommendations are based on pooled results across observational studies in women receiving cryotherapy.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of cryotherapy for the treatment of cervical intraepithelial neoplasia (CIN)

Potential Harms

- There was very low-quality evidence for the occurrence of spontaneous abortions and infertility but the risk appeared similar to that in the general population.
- There may be little difference in serious adverse events between cryotherapy and loop electrosurgical excision procedure (LEEP), but there may be fewer minor adverse events (such as pain) with cryotherapy.

Special Populations: Pregnant Women

The available limited evidence does not suggest that cryotherapy increases risk of adverse pregnancy outcomes when performed during pregnancy; however, an increased risk of pregnancy loss cannot be ruled out and evidence is required.

Qualifying Statements

Qualifying Statements

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Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

World Health Organization (WHO). WHO guidelines: use of cryotherapy for cervical intraepithelial neoplasia. Geneva (Switzerland): World Health Organization (WHO); 2011. 28 p. [94 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011

Guideline Developer(s)

World Health Organization - International Agency

Source(s) of Funding

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Guideline Committee

World Health Organization (WHO) Steering Committee for the Recommendation on the Use of Cryotherapy for Cervical Intraepithelial Neoplasia

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Financial Disclosures/Conflicts of Interest

All experts who participated in the development of *World Health Organization guidelines: use of cryotherapy for cervical intraepithelial neoplasia*, were required to complete the World Health Organization (WHO) Declaration of Interests form. Out of all the experts who participated in this work, three experts declared an interest in the subject related to cervical cancer prevention, as follows:

Dr Lynette Denny: from 2006 to 2010, she has spoken on human papillomavirus (HPV) vaccination at various speaker's fora organized by the companies Merck, Sharp & Dohme (MSD) and GlaxoSmithKline (GSK). The total honorarium received by Dr Denny from both companies combined was approximately US$3000 per year."

Dr Swee Chong Queck: over the past four years, he has participated in medical advisory boards and speakers' bureaux relating to cervical cancer prevention strategies, HPV vaccine efficacy studies and clinical relevance of HPV vaccination for the prevention of cervical cancer and other HPV related diseases. The total income received by Dr Queck from both companies combined was approximately 5000 Singapore dollars per year over the past four years.

Dr Vivien Tsu: her employer, PATH, an international nonprofit organization operating in the field of health, has received large-scale donations of HPV vaccines and test kits, as well as equipment, for use in demonstration projects aimed at promoting public health, including in particular in low-resource countries.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization Web site .

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

Availability of Companion Documents

The following is available:

- Use of cryotherapy for cervical intraepithelial neoplasia. Evidence base. Geneva (Switzerland): World Health Organization (WHO); 2011 Mar. 26 p. Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization (WHO) Web site .
- WHO handbook for guideline development. Geneva (Switzerland): World Health Organization (WHO); 2008 Mar. 41 p. Electronic copies: Available in PDF from the WHO Web site .

An executive summary is also available in the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 9, 2012.

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